

The rationale for colorectal cancer screening programs is that the removal of adenomatous polyps will prevent colorectal cancer, and that earlier detection of localized, superficial cancers in asymptomatic individuals will increase the surgical cure rate. Such screening programs are particularly important for individuals with a family history of the disease in first-degree relatives. The relative risk for developing colorectal cancer increases to 1.75 in such individuals and may be even higher if the relative was afflicted before age 60. The prior use of proctosigmoidoscopy as a screening tool was based on the observation that 60% of early lesions are located in the rectosigmoid. For unexplained reasons, however, the proportion of large-bowel cancers arising in the rectum has been decreasing during the past several decades, with a corresponding increase in the proportion of cancers in the more proximal descending colon. As such, the potential for proctosigmoidoscopy to detect a sufficient number of occult neoplasms to make the procedure cost-effective has been questioned.

Screening strategies for colorectal cancer that have been examined during the past several decades are listed in [Table 110-3](#).

Many programs directed at the early detection of colorectal cancers have focused on digital rectal examinations and fecal occult blood (i.e., stool guaiac) testing. The digital examination should be part of any routine physical evaluation in adults older than age 40 years, serving as a screening test for prostate cancer in men, a component of the pelvic examination in women, and an inexpensive maneuver for the detection of masses in the rectum. However, because of the proximal migration of colorectal tumors, its value as an overall screening modality for colorectal cancer has become limited. The development of the fecal occult blood test has greatly facilitated the detection of occult fecal blood. Unfortunately, even when performed optimally, the fecal occult blood test has major limitations as a screening technique. About 50% of patients with documented colorectal cancers have a negative fecal occult blood test, consistent with the intermittent bleeding pattern of these tumors. When random cohorts of asymptomatic persons have been tested, 2–4% have fecal occult blood-positive stools. Colorectal cancers have been found in <10% of these “test-positive” cases, with benign polyps being detected in an additional 20–30%. Thus, a colorectal neoplasm will not be found in most asymptomatic individuals with occult blood in their stool. Nonetheless, persons found to have fecal occult blood-positive stool routinely undergo further medical evaluation, including sigmoidoscopy and/or colonoscopy—procedures that are not only uncomfortable and expensive but also associated with a small risk for significant complications. The added cost of these studies would appear justifiable if the small number of patients found to have occult neoplasms because of fecal occult blood screening could be shown to have an improved prognosis and prolonged survival. Prospectively controlled trials have shown a statistically significant reduction in mortality rate from colorectal cancer for individuals undergoing annual stool guaiac screening. However, this benefit only emerged after >13 years of follow-up and was extremely expensive to achieve, because all positive tests (most of which were falsely positive) were followed by colonoscopy. Moreover, these colonoscopic examinations quite likely provided the opportunity for cancer prevention through the removal of potentially premalignant adenomatous polyps

because the eventual development of cancer was reduced by 20% in the cohort undergoing annual screening.

With the appreciation that the carcinogenic process leading to the progression of the normal bowel mucosa to an adenomatous polyp and then to a cancer is the result of a series of molecular changes, investigators have examined fecal DNA for evidence of mutations associated with such molecular changes as evidence of the occult presence of precancerous lesions or actual malignancies. Such a strategy has been tested in more than 4000 asymptomatic individuals whose stool was assessed for occult blood and for 21 possible mutations in fecal DNA; these study subjects also underwent colonoscopy. Although the fecal DNA strategy suggested the presence of more advanced adenomas and cancers than did the fecal occult blood testing approach, the overall sensitivity, using colonoscopic findings as the standard, was less than 50%, diminishing enthusiasm for further pursuit of the fecal DNA screening strategy.

The use of imaging studies to screen for colorectal cancers has also been explored. Air contrast barium enemas had been used to identify sources of occult blood in the stool prior to the advent of fiberoptic endoscopy; the cumbersome nature of the procedure and inconvenience to patients limited its widespread adoption. The introduction of computed tomography (CT) scanning led to the development of virtual (i.e., CT) colonography as an alternative to the growing use of endoscopic screening techniques. Virtual colonography was proposed as being equivalent in sensitivity to colonoscopy and being available in a more widespread manner because it did not require the same degree of operator expertise as fiberoptic endoscopy. However, virtual colonography requires the same cathartic preparation that has limited widespread acceptance of endoscopic colonoscopy, is diagnostic but not therapeutic (i.e., patients with suspicious findings must undergo a subsequent endoscopic procedure for polypectomy or biopsy), and, in the setting of general radiology practices, appears to be less sensitive as a screening technique when compared with endoscopic procedures.

With the appreciation of the inadequacy of fecal occult blood testing alone, concerns about the practicality of imaging approaches, and the wider adoption of endoscopic examinations by the primary care community, screening strategies in asymptomatic persons have changed. At present, both the American Cancer Society and the National Comprehensive Cancer Network suggest either fecal occult blood testing annually coupled with flexible sigmoidoscopy every 5 years or colonoscopy every 10 years beginning at age 50 in asymptomatic individuals with no personal or family history of polyps or colorectal cancer. The recommendation for the inclusion of flexible sigmoidoscopy is strongly supported by the recently published results of three randomized trials performed in the United States, the United Kingdom, and Italy, involving more than 350,000 individuals, which consistently showed that periodic (even single) sigmoidoscopic examinations, after more than a decade of median follow-up, lead to an approximate 21% reduction in the development of colorectal cancer and a more than 25% reduction in mortality from the malignant disease. Less than 20% of participants in these studies underwent a subsequent colonoscopy. In contrast to the cathartic preparation required before colonoscopic procedures, which is only performed by highly trained specialists, flexible sigmoidoscopy requires only an enema as preparation and can be accurately performed by nonspecialty physicians or physician-extenders. The randomized screening studies using flexible sigmoidoscopy led to the estimate that approximately 650 individuals needed to be screened to prevent one colorectal cancer death; this contrasts with the data for mammography where the number of women needing to be screened to prevent one breast cancer death is 2500, reinforcing the efficacy of endoscopic surveillance for colorectal cancer screening. Presumably the benefit from the sigmoidoscopic screening is the result of the identification and removal of adenomatous polyps; it is intriguing that this benefit has been achieved using a technique that leaves the proximal half of the large bowel unvisualized.

It remains to be seen whether surveillance colonoscopy, which has gained increasing popularity in the United States for colorectal cancer screening, will prove to be more effective than flexible sigmoidoscopy. Ongoing randomized trials being conducted in Europe are addressing

TABLE 110-3 SCREENING STRATEGIES FOR COLORECTAL CANCER

Digital rectal examination
Stool testing
• Occult blood
• Fecal DNA
Imaging
• Contrast barium enema
• Virtual (i.e., computed tomography colonography)
Endoscopy
• Flexible sigmoidoscopy
• Colonoscopy